AUSTRALIAN PATENT OFFICE
SEARCH REPORT

Applicant's or agent's file reference 200130790/030423/TMSR/3220		
Application No. SG 200103079-0	Application Filing Date *(day/month/year)* 22 May 2001	(Earliest) Priority Date *(day/month/year)* 17 July 2000
Applicant WANG, XIAO BING et al		

This search report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. [ ] **Certain claims were found unsearchable** (See Box I)

2. [ ] **Unity of invention is lacking** (See Box II)

3. [ ] The application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the search was carried out on the basis of the sequence listing

   [ ] filed with the application

   [ ] furnished by the applicant separately from the application,

   [ ] but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in application as filed

4. With regard to the **title**,

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Office to read as follows:

5. With regard to the **abstract**,

   [X] the text is approved as submitted by the applicant

   [ ] the text has been established by this Office as it appears in Box III

6. The figure of the **drawings** to be published with the abstract is Figure No.

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure

   [ ] because this figure better characterises the invention

   [X] None of the figures

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Application No.
SG 200103079-0

A. CLASSIFICATION OF SUBJECT MATTER

According to International Patent Classification (IPC)

Int. Cl. [7] C12Q 1/68

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

SEE BELOW

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SEE BELOW

Electronic data base consulted during the search (name of data base and, where practicable, search terms used)

CA, WPIDS, MEDLINE: mutation, single nucleotide primer extension, primer oligo base extension, mutation, primer, 3', downstream, upstream, flanking, 5'

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 30545 A (APPLIED GENETICS, INC.) 3 October 1996 See in particular pages 8 and 16	1-30
X	Braun A et al (1997) "Detecting CFTR gene mutations by using primer oligo base extension and mass spectrometry" Clinical Chemistry 43(7), pages 1151-8 See in particular page 1153, column 1 and figure 1, parts (b) and (c).	1-30

[X] Further documents are listed in the continuation of Box C

[X] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of submission of the request to the Australian Patent Office	Date of completion of the search report	Date of mailing of the search report
28 April 2003	28 May 2003	02 JUN 2003

Name and mailing address	Authorised officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. 61 2 62853929	TERRY MOORE

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C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 888 819 A (GOELET P et al) 30 March 1999 See whole document	All claims
A	WO 91 13075 A (ORION-YHTYMÄ OY) 5 September 1991 See whole document	All claims
A	Prezant TR et al (1992) "Trapped-oligonucleotide nucleotide incorporation (TONI) assay, a simple method for screening point mutations" Human Mutation 1, pages 159-64 See whole document	All claims
A	Piggee CA et al (1997) "Capillary electrophoresis for the detection of known point mutations by singel-nucleotide primer extension and laser-induced fluorescence detection" J Chromatography A, 781, pages 367-75 See whole document	All claims

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SEARCH REPORT

PATENT FAMILY MEMBERS

Application No.
SG 200103079-0

Patent Document Cited in Search Report		Patent Family Member					
WO	96 30545	AU	52964/96	EP	751951		
US	5888819	AU	15848/92	EP	576558	WO	92 15712
WO	91 13075	AU	72351/91	EP	648280	HU	61330

END OF ANNEX

AUSTRALIAN PATENT OFFICE

WRITTEN OPINION

	Date of mailing *day/month/year* 02 JUN 2003
Applicant's or agent's file reference 200130790/030423/TMSR/3220	**REPLY DUE** within FIVE MONTHS of the date of the Registrar's letter enclosing the written opinion

Application No.	Application Filing Date *(day/month/year)*	Priority Date *(day/month/year)*
SG 200103079-1	22 May 2001	17 July 2000

International Patent Classification (IPC) (as indicated in the search report)

Int. Cl. [7] C12Q 1/68

Applicant

WANG, XIAO BING et al

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1. This first written opinion consists of a total of 5 sheets.
2. This opinion contains indications relating to the following items:.

I	[X]	Basis of the opinion
II	[ ]	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
III	[ ]	Lack of unity of invention
IV	[X]	Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
V	[ ]	Certain documents cited
VI	[ ]	Certain defects in the application
VII	[X]	Certain observations on the application

3. This opinion is based upon the assumption that the priority claim is valid.
4. The search report used was issued by the **Australian Office**, and the date of completion is: **28 May 2003**
5. If no reply is filed, the examination report will be established on the basis of this opinion.
6. The date by which the examination report will be established is: **17 October 2004**

Name and mailing address	Authorized Officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile no. 61 2 62853929	TERRY MOORE

AUSTRALIAN PATENT OFFICE

WRITTEN OPINION

Application No.

SG 200103079-1

I. Basis of the opinion

1. This opinion has been drawn on the basis of:

[X] the application as originally filed.

[ ] the description, pages , as originally filed,
pages , filed with the request,
pages , received on with the letter of

[ ] the claims, pages , as originally filed,
pages , filed with the request,
pages , received on with the letter of

[ ] the drawings, sheets/fig. , as originally filed,
sheets/fig. , filed with the request,
sheets/fig. , received on with the letters of

[ ] the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. The amendments have resulted in the cancellation of: pages:
sheets of drawings/figures No :

3 [ ] This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box.

4. Additional observations, if necessary:

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WRITTEN OPINION

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IV. Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims **19-22 and 28-30**	YES
	Claims **1-18, 23-27 and 31-36**	NO
Inventive step (IS)	Claims	YES
	Claims **1-36**	NO
Industrial applicability (IA)	Claims **1-36**	YES
	Claims	NO

2. Citations and explanations

The invention described in the specification resides in a method of detecting or quantifying a target nucleic acid sequence with respect to a specific base change in the sequence. The method broadly involves the use of primer that is complementary to the target sequence and that anneals to the target sequence immediately upstream of the specific base. Primer extension is then conducted using a mix comprising:

(i) one type of ddNTP, or an absence of the any nucleotide complementary to the specific base, and

(ii) the remaining three types of dNTPs that are different to the complement of the specific base, any of which may be optionally labelled.

Novelty and Inventive Step

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1 WO 96 30545
D2 Braun et al
D3 US 5 888 819
D4 WO 91 13075
D5 Prezant et al
D6 Piggee et al

D1 discloses a method for detecting or quantifying a target nucleic acid sequence with respect to base changes at a specific location. In particular the method is used to assess mutations in the human COX1 gene, but it is also discloses that the method is suitable for a broad range of nucleic acids. D1 discloses use of a primer that whose 3' end is immediately adjacent to the base of interest. The primer is extended using a polymerase and a mix comprising one type of ddNTP, or an absence of nucleotide corresponding to the complement of the base of interest and from one to three of the remaining three types of nucleotide that are different to the complement of the specific base. The ddNTP and/or the dNTPs may optionally be labelled. As such the citation deprives claims 1-18, 23, 24, 27 and 31-36 of novelty.

With respect to the remaining claims, features such as those that enable attachment to a solid support, use of nucleotide analogues and extragenomic samples simply represent routine applications of the disclosed method that are standard in the art. As such these claims lack an inventive step.

Continued on supplemental sheet

Supplemental Box
(To be used when the space in any of Boxes I to VII is not sufficient)

Continuation of Box [No.]: IV2

D2 discloses a further method using a primer that anneals immediately adjacent to the base of interest and primer extension using a mix comprising the ddNTP corresponding to the complement of the base interest and three dNTPs that are different to the complement of the base of interest. The method is used to assess mutations in the CFTR gene.

In particular figure 1(b) discloses the F508C mutation and the use of ddCTP as the chain terminator and 1(c) discloses the G542X mutation using ddTTP. The citation also discloses affinity capture of PCR products on solid phase and the use of modified nucleoside analogues. As such the citation deprives claims 1-6, 10-13, 23-27 and 31-36 of novelty.

Furthermore, as discussed with respect to D1, the subject matter of the remaining claims appears to represent nothing more than routine application of the method disclosed in the citation. As such, the remaining claims lack an inventive step in light of D2

D3-D6 all disclose similar methods to those disclosed in the specification. However D3 and D6 use only ddNTPs corresponding to the base of interest, with no added dNTPs and D4 and D5 disclose only dNTPS, with no added ddNTPs. As such none of D3-D6 appear to disclose or teach toward the subject matter of the claims.

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VII. Certain observations on the application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

[X] The claimed invention is patentable according to Section 13(2); or

[ ] The claimed invention is unpatentable according to Section 13(2) because: